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10/566,100	10/26/2006	Antoni Torrens Jover	283628US0PCT	9565

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
12/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/566,100	TORRENS JOVER ET AL.	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 30-63* is/are pending in the application.

4a) Of the above claim(s) *54-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 30-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 10/21/2010 amending claims 1-5, 30-53 and adding new claims 54-63. Claims 6-29 have been canceled. Claims 1-5, 30-63 are pending. Claims 54-63 are withdrawn from consideration because they do not read on the elected species 'regulation of appetite'. Claims 1-5, 30-53 are examined on the merits herein.

Response to Remarks

Applicants' amendments necessitated the withdrawal of the 112(1) solvate, 112(1) written description, 112(2), 101 rejections. Applicants' arguments regarding the ODP rejection against 10/565979 have been fully considered and the rejection is withdrawn. Applicants' arguments regarding the other ODP and 103(a) rejections have been fully considered and found not to be persuasive. Hence the ODP and 103 rejections are modified (due to Applicants' amendments) and are given below for Applicants' convenience. Applicants' amendments necessitated the new 112(1) rejection presented in this action. Applicants' arguments regarding the rejections are addressed below. The action is made Final.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 30-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-9, 34-45 of copending Application No. 10/566,402. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the co-pending application teaches an active substance combination of at least one compound with neuropeptide receptor NPY affinity of formula I a with at least one compound with 5-HT6 receptor affinity of formula I b and further claims the use of such compounds in treating various disorders including regulation of appetite (elected species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 4 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 19-23 of copending Application No. 10/566,399 in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3, 4 and 30-53 are towards the pharmaceutical composition or compounds comprising 1, 4 disubstituted piperidines of compounds of formula I and at least one compound with 5-HT6 receptor affinity of formula I b.

The claims of the co-pending application '399 are towards the pharmaceutical composition or medicament of some of the compounds comprising 1, 4 disubstituted piperidines compounds as instantly claimed and the use of such compositions in regulation of appetite, obesity, CNS disorders etc.

Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the co-pending application with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Merce-Vida and Caldirola. Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS, obesity disorders etc.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-5 and 30-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 18 of U.S

Patent No. 7,056,914 in view of Jover et al. (US 2004/0058920) and further in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-5 and 30-53 are towards the pharmaceutical composition or the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders etc.

The claims of the patent are towards the pharmaceutical composition or medicament of the compounds comprising 1, 4 disubstituted piperidines compounds as instantly claimed.

The co-pending application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Jover et al, Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the patent with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches that 1,4 disubstituted piperidine compounds of the patent has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity

because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claims 1, 3-5 and 30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 of U.S Patent No. 7,041,665 in view of Jover et al. (US 2004/0058920) and further in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-5 and 30-53 are towards the pharmaceutical composition or the compounds comprising 1,4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders etc.

The claims of the patent are towards the pharmaceutical composition of the compounds comprising 1, 4 disubstituted piperidines compounds as instantly claimed.

The patent application does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Jover et al, Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the patent with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches that 1,4 disubstituted piperidine compounds of the patent has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious

to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claims 1, 3-4 and 30-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S Patent No. 7,514,429 in view of Merce-Vidal et al. (U.S. 7,105,515) and Caldirola et al. (U.S. 7,144,883).

Claims 1, 3-4 and 30-53 are towards the pharmaceutical composition or the compounds comprising 1, 4 disubstituted piperidines of compounds of formula I a and at least one compound with 5-HT6 receptor affinity of formula I b and the use of such compositions in various disorders including regulation of appetite, CNS disorders, pain, depression, epilepsy, anxiety, depression, hypertensive syndrome disorder, diabetes, food digestion disorders etc

The claims of the patent are towards the method of use of the compounds comprising 1,4 disubstituted piperidines compounds as instantly claimed and the use is towards treating food digestion disorders, obesity, bulimia, pain, depression, anxiety, hypertensive syndrome, diabetes etc

The patent does not teach an active substance combination with at least one additional compound with 5-HT6 receptor affinity of formula I b.

Merce-Vidal and Caldirola et al. teachings discussed as above.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the patent with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Merce-Vidal. Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a formulation or a combination of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a combination of at least one compound with neuropeptide receptor Y (NPY) affinity (formula I a) and at least one compound with 5-HT6 receptor affinity (formula I b) or a composition comprising the same or the use of such composition or combination for prophylaxis or treatment of various disorders including regulation of appetite, Alzheimer's, Parkinson's,

arthritis, cachexia, bulimia, anorexia etc. The claims are very broad in scope with respect to the number of compounds in combination, in preparation of the pharmaceutical composition and use of such combination or combination in treating myriad of unrelated diseases. The specification provides guidance to synthesis of the compounds that bind to NPY receptor and binding results for some of the representative compounds of formula (Ia-Ih) to NPY receptor and 5-HT6 receptor. The specification in p 421 states that "Both combinations show a synergic effect in their pharmacological activities compared with the individual pharmacological activity for each compound" referring to the combination of the elected species and one other combination. The results were measured for food ingestion. The specification does not indicate what the effective amount is or what amounts of such combination was effective in food ingestion. Applicants have claimed a large number of compounds in combination and further claim such combination in treating a large number of distinct and etiologically different disorders such as regulation of appetite and Parkinson's disease. The results stated by the Applicants here does not commensurate in scope with respect to the all the amounts, the combinations and for all the disorders claimed. The amended claim 4, has a limitation that 'the composition in an amount sufficient for". There is no guidance in the specification what will be the sufficient amount of compound A with compound B for treating different disorders. The sufficient amount of compound A with compound B for regulation of appetite may not be the same for treating Parkinson's disease. The specification does not provide any guidance for treatment of any of the disorders claimed. If compounds are used in a combination for therapy the formulations

comprising the active agents can be used in different formulations (e.g. for sequential administration) or in a single formulation. If the medicament with the active agents is in a single pharmaceutical formulation then a person of ordinary skill in the art has to do an undue experimentation to prepare such a combination with the active substances claimed as in combination therapy potential drug interactions, toxicity measurements etc need to be considered. Applicants' have claimed the same combination of compounds for treating various disorders such as bulimia and anorexia. It is not predictable from the guidance given by the Applicants' (synthesis of the compounds with NPY receptor affinity and binding affinity for some representative samples of the compounds synthesized) that the same composition is manufactured for treating obesity and bulimia. It is not predictable from the guidance given by the Applicants' that the same pharmaceutical formulation is manufactured for treating cardiovascular disorders and Alzheimer's. It is hard to predict whether the same composition is used in treating various disorders claimed because each disease has a different and distinct etiology and pathophysiological manifestations, and that each is differently treated. Applicants' have not provided any guidance to making any of the pharmaceutical compositions with active substances in combination. It is not clear from the specification whether any amount of active substance that has neuropeptide receptor affinity (formula I a) in combination with any amount of a compound that has 5-HT6 receptor affinity (formula I b) will simultaneously regulate neuropeptide Y and 5-HT6 receptor. It would be an undue experimentation for a person of ordinary skill in the art to find the effective amount of combination of all the compounds of A and B in treating all the unrelated

disorders claimed. A skilled artisan would not recognize that Applicants' were in possession of the claimed invention of composition comprising an active substance combination for simultaneous neuropeptide Y and 5-HT6 receptor regulation and the use of such combination in treatment for regulation of appetite, for maintenance, increase or reduction of body weight; for a disorder related to food ingestion; for obesity, anorexia, cachexia, bulimia, diabetes, type II diabetes (non-insulin-dependent diabetes mellitus), a gastrointestinal tract disorder, irritable bowel syndrome, a peripheral nervous system disorder, a central nervous system disorder, arthritis, epilepsy, anxiety, panic, depression, a cognitive disorder, a memory disorder, or for improvement of cognition; for a cardiovascular disease, senile dementia, Alzheimer's disease, Parkinson's disease, Huntington's disease, schizophrenia, psychosis, infantile hyperkinesia (ADHD, attention deficit/hyperactivity disorder), pain, hypertensive syndrome, an inflammatory disease; or for an immunologic diseases.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

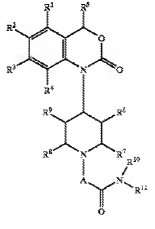
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the

various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 30-33, 42-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jover, et al. (US 2004/0058920, filing date Apr 4 2003) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002).

Jover et al. teaches benzoxazinone- derived compounds of formula I as claimed in the instant application, their compositions and their use as a medicament in treatment of humans or animals (see abstract, para 0010). The reference teaches A can be CH2 (para 0015), R10 can H and R11 can be heteroaryl radical (para 0017), then it can read on the elected species.

(I)



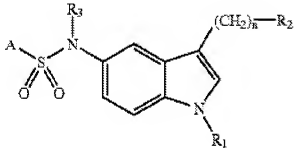
The reference further teaches that the compositions comprising the compound can be formulated into orally administrable form containing one or more physiologically compatible carriers or excipients, and may take any convenient form, such as tablets, pellets, capsules, lozenges, aqueous or oily solutions, suspensions, emulsions, or dry powdered form suitable for reconstitution with water or other suitable liquid medium before use, for immediate or controlled release (para 0288). The reference teaches the compounds as neuropeptide Y receptor regulators are useful for the regulation of food ingestion (para 009) and in the treatment of treatment of disorders of food ingestion, preferably obesity, anorexia or bulimia (para 0285). In para 003, the reference teaches that NPY (neuropeptide Y) is a powerful stimulant of food ingestion and thus appetite is significantly increased when NPY is injected directly into the CNS of satiated mice.

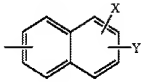
It would have been obvious to one having ordinary skill in the art at the time of the invention to have used compounds of formula I a in regulation of appetite because of the teachings of Jover et al. Jover et al. teaches that NPY (neuropeptide Y) is a powerful stimulant of food ingestion and thus appetite is significantly increased and further teaches that the compounds of formula I a can be used in regulation of food ingestion. Thus it would have been obvious to one having ordinary skill in the art to have used the claimed compounds in regulation of appetite because the compound are taught to be NPY regulators and NPY regulation regulates the appetite according to Jover et al. One having ordinary skill in the art would have been motivated to use the compounds in a method of regulation of appetite in order to treat the food ingestion disorders including obesity, bulimia etc.

The reference does not teach a 5-HT6 receptor affinity compound in the active substance combination.

The reference Merce-Vidal teaches derivatives of sulphonamides (see abstract).

(I)





When R1=H, n=0, A= , R3=H the reference teaches the elected species for 5-HT6 (see col. 2, lines 50, 65, 67, col. 3, line 24). The reference provides guidance towards the synthesis of the sulfonamide compounds, its pharmaceutical formulation the amount of daily doses (1-500 mg) in human medicine (see col. 33, lines 55-67, col. 34, example 1). Merce-Vidal teaches that the compounds have 5-HT6 serotonin receptor antagonistic activity useful in the preparation of medicament for prevention or treatment of various CNS (central nervous system) disorders.

Caldirola et al. teaches substituted sulfonamide compounds with 5-HT6 receptor affinity to be useful for the prophylaxis and treatment of medical conditions relating to obesity, type II diabetes and/or disorders of the central nervous system (see abstract, col. 2, lines 31-35). The reference teaches preparation of such compounds,

pharmaceutical formulations and a method of using such compounds in treating obesity (col. 107, claims 7-9).

It would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a compound of the instantly claimed with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover and Merce-Vidal. Jover teaches some of the instantly claimed compounds as NPY affinity compounds and can be used in treating CNS disorders. Merce-Vidal teaches 5-HT6 compounds as claimed including the elected species. Merce-Vidal and Caldirola et al. teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation or a medicament of at least one compound of the instantly claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating CNS disorders. One having ordinary skill in the art would have been motivated in making such a medicament combination in expectation of using the same in a method of treating CNS disorders. One of ordinary skill in the art would have been motivated to incorporate the two agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat a CNS disorder or obesity individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069. It would have been obvious to one having ordinary skill in the art at the time of the invention to have manufactured the medicament combining NPY receptor affinity

compound with 5HT-6 receptor affinity compound to use in regulation of appetite because the prior art shown above teaches the preparation of pharmaceutical formulations of the active medicaments and their use in treating obesity. Obesity is an eating disorder and a root cause for obesity is excessive consumption of food. Appetite is a desire to eat food when hungry and abnormal appetite could lead to an eating disorder, obesity. Hence treating obesity condition leads to suppression of appetite or regulation of appetite. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a medicament comprising an active substance combination of a compound with neuropeptide receptor affinity with that of a compound with 5-HT6 serotonin receptor affinity or use of the combination for the manufacture of a medicament for simultaneous neuropeptide Y5 and 5-HT6 regulation. The references do not explicitly teach the amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compound for active substance combination or in a medicament. However, the references in general teaches dosage amounts of NPY receptor affinity compound and 5-HT6 receptor affinity compounds in making formulations or medicaments and in the manufacture of the same. It would have been obvious to one of ordinary skill in the art at the time of the invention to have adjusted the amounts of component A and component B as claimed by the Applicants (claim 4) through routine experimental procedure. Generally, the ratios of concentration will not support the patentability unless there is evidence indicating such concentration is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to

discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955).

Claims 34-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jover et al. (US 2004/0058920, filing date Apr 4 2003) in view of Merce-Vidal et al. (U.S. 7,105,515, effective filing date Nov 13 2002) and Caldirola et al. (U.S. 7,144,883, effective filing date, June 11 2002) as applied to claims 1-5, 30-33 above and further in view of Noda et al. (U.S. 5,320,853).

Jover, Merce-Vidal et al. and Caldirola et al teachings discussed as above.

The references do not teach the pharmaceutical formulation in a sustained release form.

Noda et al. teaches controlled release formulation for pharmaceutical compounds. The reference teaches a coat and sustainable drug releasing exterior coat (see Abstract). The reference teaches water insoluble polymers including ethylcellulose, cellulose acetate (col.2, lines 40-45), drug releasing polymers such as acrylates and/or methacrylates (Eudagrit) (col. 5, lines 10-20, col. 6, lines 55-65), plasticizers (col. 5, lines 37-40) and white wax (also known as beeswax) (col. 9, line 8) in the sustained release formulation.

It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a controlled release drug delivery device with combination of a compound of the instantly claimed with that of a compound with 5-HT6 serotonin receptor affinity because it within the knowledge of the skilled pharmacologist to make differential release composition as they represent conventional formulations and modes

of administration. It is well known from the prior art teachings like Noda et al. that such conventional formulations can be made. One having ordinary skill in the art at the time of the invention would have been motivated to make a controlled release formulation of the active substance combination claimed in order for once or twice a day administration of the drugs and achieve desired blood levels of the drugs in a manner which delays or sustains the release of the drug. It would have been obvious to one having ordinary skill in the art to formulate a composition where one of the components (A) or (B) as claimed is in a non-sustained release dosage form is in case of a medical condition where one of the components needs to be delivered without any controlled drug delivery.

Response to Arguments

(1) ODP rejections:

(a) Provisional ODP rejections: Applicants argue that "The Applicants' submit that the foregoing amendments and remarks address all the remaining rejections and place this application in condition for allowance. Accordingly, this provisional double patenting rejection can be withdrawn" with respect to the provisional ODP rejections. However Applicants' arguments do not overcome the rejections. Hence the provisional ODP rejections are modified (due to Applicants' amendments) and are given in this office action for Applicants' convenience.

(b) ODP rejections with patents: Applicants argue that "This rejection cannot be sustained because the secondary references provide no motivation or direction for

producing the combination of the invention". In response, for the obvious double patenting rejections showing of obviousness must be provided and it is not necessary to provide a motivation to show why one of ordinary skill in the art at the time of the invention would have found it obvious to combine the patent with the secondary references. In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to have combined a 1, 4 disubstituted piperidine compounds of the patent with that of a compound with 5-HT6 serotonin receptor affinity from the teachings of Jover or Merce-Vidal and Caldirola. Jover teaches that 1,4 disubstituted piperidine compounds of the patent has neuropeptide Y (NPY) affinity and the compounds can be used in treating obesity disorders and Merce-Vidal and Caldirola teaches the use of 5-HT6 receptor binding compounds to be useful in obesity, CNS disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to have made a combination or a formulation of at least one compound of the 1, 4 disubstituted piperidine compounds claimed with at least one compound with 5-HT6 receptor affinity because both of them have been taught in the prior art to be useful in a method of treating obesity disorders.

(2) 103(a) rejections:

Applicants' argue that Jover does not teach the compound B, 5-HT6 receptor affinity compound with 1, 4 disubstituted piperidine compound (A) and do not provide motivation to combine B with A. In response, when Jover combined with the secondary references Merce-Vidal and Caldirola the combination of the compounds are taught Compounds A and compounds B are taught in the prior art references to be useful for

treating disorders such as central nervous system disorders, obesity etc. The instant application claims a combination of compound A with compound B and its use in treating disorders such as central nervous system disorders (claims 4, 5), obesity etc. As stated above a person of ordinary skill in the art would have found it obvious to make a formulation comprising two agents (here A and B) herein each of which is known to be useful to treat a CNS disorder individually into a single composition useful for the very same purpose is *prima facie* obvious. See *In re Kerkhoven* 205 USPQ 1069.

Applicants' argue that unlike the detergent mixture (see p 35 of Arguments) there will be no expectation of success when combining the compounds A and B as claimed because mixing different classes of drugs may result in antagonism, where the biochemical mechanism of one drug interferes with the biochemical mechanism mediating the effect of the other drug. In response, however a person of ordinary skill in the art would have found it obvious combining a 1, 4 disubstituted piperidine compound with a 5-HT6 receptor affinity compound because the prior art teaches that both of them are useful in treating a disorder such as CNS disorder. This provides a motivation to a person of ordinary skill in the art to combine and use them in treating a disorder such as CNS disorder. A person of ordinary skill in the art would have expected success because both types of compounds have been shown to be useful in treating the same disorders.

Applicants' state that the combination of compounds A and B exhibit synergy which is surprising to one of ordinary skill in the art. In response, it is well known in the art that when two compounds are known in the art to be useful to treat the same

disorder it would be obvious to a person of ordinary skill in the art that combining both the compounds to treat the same disorder may result in synergistic or additive therapeutic benefits. The specification in p 421 states that "Both combinations show a synergic effect in their pharmacological activities compared with the individual pharmacological activity for each compound" referring to the combination of the elected species and one other combination. The results were measured for food ingestion. Applicants have claimed a large number of compounds in combination and further claim such combination in treating a large number of distinct and etiologically different disorders such as regulation of appetite and Parkinson's disease. The results stated by the Applicants here does not commensurate in scope with respect to the all the amounts, the combinations and for all the disorders claimed.

Conclusion

No claims are allowed.

Applicant's amendment and the addition of new claims necessitated the modified and new rejections presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627